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FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
1300 I STREET, NW
WASHINGTON, DC 20005

EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 10/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/742,033	SUN ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,9-20 and 26-40* is/are pending in the application.

4a) Of the above claim(s) *39 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4,9-20 and 26-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. The Response filed July 13, 2004 is acknowledged. As noted in the 6/16/04 Response, the finality of the previous action (i.e., Paper No. 14) has been withdrawn.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

3. Claims 3, 4, 9-20, 22-34 were pending. Applicants canceled claims 22-25 and amended claims 3, 4 and 14. In addition, Applicants added claims 35-40. Therefore, claims 3, 4, 9-20, 26-40 are currently pending.

4. Newly added claims 39-40 are drawn to non-elected species and/or inventions (e.g., see 7/13/04 Response) and thus these claims remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), there being no allowable generic claim.

5. Therefore, claims 3, 4, 9-20, 26-38 are examined on the merits in this action.

Priority

6. Applicants' state, "Claims 3-4, 10-13, 17-20, 22 and 26-34 are fully supported by the disclosure of U.S.S.N. 08/484,766 ['766 application] ... and have apriority date of no later than

June 7, 1995." The Examiner respectfully disagrees. The '766 application is drawn to an electrochemiluminescence (referred to herein as "ecl") assay using, for example, an enzyme linked antibody to visualize antigens to which said antibody binds via the enzyme linked hydrolysis of a penicillin substrate conjugated to various metal complexes like (bipyridyl)ruthenium(II) (referred to herein as "$Ru(bpy)_3^{2+}$") to yield an activated ecl complex (referred to herein as "hydrolyzed Ru-Amp or Ru-APA"). However, the '766 application never mentions (i.e., provides no support for) the use of a "co-reactant" that can be "on exposure of said compound to electrochemical energy sufficient to from said reductant or said oxidant, said reductant or oxidant reacts with said label so as to cause said label to emit electrochemiluminescence" (e.g., see claim 3, step ii) i.e., ***it does not appear that Applicants' ever had conception of this broader genus***. In addition, there is no mention (i.e., no support) of the use of "amines" including primary, secondary and tertiary "aliphatic" amines such as "dipropyl or N,N-dipropyl" amine (e.g., see claims 13-16). In addition, other co-reactants like "NADH" are also not supported (e.g., see claim 17).

The '766 application does provide an example that might fall within the scope of a co-reactant that is hydrolyzed to form a β-lactam antibiotic having a hydrolyzed β-lactam bond" (e.g., see claim 40), however, ***this conjugate has been expressly excluded from the scope of Applicants' claims in the specification*** (e.g., see specification page 15, paragraph 2, "It should be noted that 'electrochemiluminescence coreactant' and 'ECR' as used herein do not include species known as 'chemically transformable first compound' ('CTFC') as that term is used in U.S. Pat. No. 5,643,713 issued Jul. 1, 1997 (which is incorporated by reference) ... which undergoes a structural transformation in response to chemical stimulus, e.g., hydrolysis ... which

transformation alters the measurable luminescence of a detectable ECL compound containing the CTFC in comparison to the measurable luminescence before any such transformation has occurred. For instance, the CTFC can be an enzyme substrate ... The enzyme substrate can be a beta-lactam, such as (D), and the enzyme its corresponding beta-lactamase"). Here, the '766 application to which Applicants claim priority also disclose a "beat-lactam" that undergoes "hydrolysis" which "alters the measurable luminescence of a detectable ECL compound containing the CTFC in comparison to the measurable luminescence before any such transformation [i.e., hydrolysis] has occurred." Thus, the '766 application provides no support whatsoever for the currently claimed invention because it expressly disclaims the only compound disclosed in '766 that might otherwise fall within the scope of the claims. The Examiner further notes that Applicants have not pointed to any passages in '766 that provide support for these claims (e.g., Applicants have not provided any page and line numbers).

Withdrawn Objections/Rejections

7. All previous rejections under 35 U.S.C. 112, second paragraph are withdrawn in view of Applicants' arguments and/or amendments. The New Matter rejection under 35 U.S.C. 112, first paragraph is withdrawn in view of Applicants' arguments and/or amendments. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claims Rejections - 35 U.S.C. 101

8. Claims 3, 4, 9-20, 26-38 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 3, 4, 9-20 and 26-38 recite both a "product" and a "method of use" (see 35 U.S.C. 112, second paragraph rejection below). However, Applicants may only obtain "a" patent i.e., one (1) patent for a "product" OR a "method of use", not a hybrid claim drawn to a product AND a method of use.

The Examiner concedes that there are situations where claims are permissively drafted to include a reference to more than one statutory class of invention (e.g., see MPEP § 2173.05(p) disclosing "product-by-process" claims), but the Examiner notes that those situations are only permissible because Applicants make clear that the "product" and NOT the "process" is being claimed (e.g., see MPEP § 2173.05(p), "A claim to a device, apparatus, manufacture, or composition of matter may contain a reference to the process in which it is intended to be used ... so long as it is clear that the claim is directed to the product and not the process") (emphasis added). Here, it would appear that both the "product" and the "method of use" are simultaneously being claimed.

Response

9. Applicant's arguments directed to the above 35 U.S.C. § 101 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue, "The Examiner misinterprets a chemical property of the co-reactant described as 'coreactant undergoes oxidation to form a reductant or reduction to form an oxidant' for a statement of intended use. (See claim 3 before present amendment) ... thus, the limitation is

not an 'intended use' limitation. However, to further prosecution of the application, Applicants have amended claims 3 and 4 to further emphasize that the limitation is a required property or characteristic of the claimed compound" (e.g., see 11/24/03 Response, page 40, section K).

This is not found persuasive for the following reasons:

The Examiner contends that Applicants' amendments have only exacerbated this problem. The current amendment states, "on exposure of said compound to electrochemical energy ... said reductant or oxidant reacts with said label" (e.g., see newly amended claim 3). Here, the Examiner contends that Applicants have not "made clear" whether the product or the "method" is being claimed because limitations like "on exposure of said compound to electrochemical energy sufficient to form said reductant or said oxidant" and "said reductant or oxidant reacts with said label so as to cause said label to emit electrochemiluminesce" (e.g., see claim 3) can reasonably be interpreted as method steps (e.g., a method consisting of the following steps [1] expose said compound to electrochemical energy and [2] react said reductant or oxidant with said label; see also 35 U.S.C. 112, second paragraph rejection below). Other dependent claims also support this interpretation (e.g., see claims 32-33 which requires an experiment to "oxidize" or "reduce" the molecule i.e., the claim doesn't require a compound that is "capable" of being reduced or oxidized but, instead, requires that the actual oxidation and/or reduction occur).

Accordingly, the 35 U.S.C. § 101 rejection cited above is hereby maintained.

Claims Rejections - 35 U.S.C. 112, first paragraph

10. Claims 3, 4, 10-20, 26-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Applicants' newly added claims are directed to a broad and highly diverse genus of electrochemiluminescent (ecl) conjugates comprising an "electrochemiluminescent label" linked presumably by a "linker" to a "coreactant" (e.g., see newly amended claim 3). These claims represent enormous scope because the ecl label (e.g., see claims 3, 4, 10-20, 26-38), linker (e.g., see claims 3, 4, 10-19, 26-27, 30-38) and/or coreactant (e.g., claims 3, 4, 10-13, 19-20, 26-35) are not structurally defined (or, in the alternative, are only "minimally" defined) and thus would include an enormous number of structural variants falling within virtually every known chemical class and subclass.

In contrast, Applicants' specification provides only a few examples of a tris-bipyridine ecl label conjugated via an alkylamine linker to several alkyl amine coreactants (see specification, Examples; see also figures 1-2; see also specification pages 13-14). With regard to adequate written description, Applicants are referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175). For adequate disclosure, like enablement, requires *representative examples*, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the full scope of the claimed invention.* See *In re Riat* (CCPA

1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure. In addition, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05).

Here, Applicants have not provided a "representative" number of examples and/or species that "reflect the variation within the genus" as required by MPEP § 2163.05 and *Lilly*. For example, Applicants' specification does not provide any examples and/or species of energy deficient systems that generate light emission via "forbidden" pathways (e.g., triplet-triplet annihilation), which would be included in Applicants' broad genus because Applicants do not "wish to be bound by a theoretical explanation of reaction mechanism" (see specification, page 11, lines 1-2). Furthermore, Applicants' teachings in the specification do not remedy this deficiency because the equation to which Applicants' refer for guidance (e.g., see specification, claims 12 wherein Applicants' disclose $\Delta G^0 = E^0(A/A-)-E^0(D+/D)$) does not apply to these energy deficient systems.

In addition, even within the much more narrowly defined subset of Applicants' most preferred embodiments there is great uncertainty and variability (e.g., see Knight et al., page 101R, column 2, "It is not the case, however, that all tertiary amine compounds take part in ECL reactions with $Ru(bpy)_3^{2+}$ [i.e., one of Applicants' preferred embodiments e.g., see figure 1-2 in specification] to produce light. Many tertiary amine compounds produce intense emission whereas other structurally related similar compounds produce virtually no ECL emission"; see

also figures 1-2 showing Applicants' preferred embodiments) (emphasis added). Knight et al. also state that a hydrogen atom attached to the α-carbon is "essential" for ECL activity (e.g., see Knight et al., Conclusion, "A hydrogen atom attached to the α-carbon is usually essential for ECL activity") because it is the α-carbon that forms the strongly reducing intermediate that is "the source of the chemical energy to produce ... the ECL reaction" (e.g., see Knight et al., paragraph bridging pages 102R-103R, Reaction Mechanism section; see also page 103R, figure 2) (emphasis added). Thus, it would appear to the Examiner that the α-carbon is required (i.e., the ECL would not be achieved without it), which clearly shows that Applicants were not in possession of alkyl amines that do not possess such an α-carbon (i.e., the full scope of the claimed invention).

Finally, the Examiner notes that Applicants' claimed invention is not defined with any chemical or physical characteristics, but only by functional properties (i.e., the ability of the coreactant to form a reductant/oxidant and then subsequently react with a label, see claims 3 and 4). Applicants are referred to the discussion in *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 285 F.3d 1013 (Fed. Cir. 2002) wherein the court adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics ***when coupled with a known or disclosed correlation between function and structure*** ... ." *Enzo*, 296 F.3d at 1324-25 (quoting Guidelines, 66 Fed. Reg. at 1106 (emphasis added)). Here, no such correlation exists between structure and

function nor is there an other identifying characteristics that would alleviate the structure/function deficiency because, as exemplified by Knight et al., studies of this nature are difficult to perform even for a much small subset of Applicants' most preferred compounds (e.g., see Knight et al., page 102R, column 1, first full paragraph, "practical difficulties arise if a range or family of compounds are to be compared to determine their relative ECL activity. Relatively small changes in the structure of compounds, e.g., a stepwise increase in alkyl chain length, will often dramatically change its solubility, [etc.] ... Hence comparisons over a range of compounds under the same experimental conditions are often not possible"). Thus, Applicants have not demonstrated in "full, clear, concise, and exact terms" that they are in possession of the "full scope" of the currently claimed invention because they have not provided a "representative" number of examples sufficient to describe the variation (or account for the unpredictability) in the genus in violation of *Lilly* and they have also impermissible used functional language without providing any structure/function relationship and/or any other identifying features in violation of *Enzo*.

Response

11. Applicant's arguments have been fully considered but they are not found persuasive. The examiner's rationale is set forth below. Please note that the above rejection has been modified to address Applicants' arguments and/or amendments and/or to include Applicants' newly added claims.

[1] Applicants argue, "there is no reasonable basis for asserting that the claims must be limited to the specific species disclosed in the specification. The original specification broadly

describes the terms 'electrochemical label' and 'coreactant' (see Specification, pp. 6 and 9) and disclose an extensive list of useful pairs and linkers (see Specification, p. 16, line 23 –p. 18, line 2)" (e.g., see 11/24/03 response, page 15, section 1).

[2] Applicants argue, "The patent need not describe what is well known in the art ... ECL labels, ECL coreactants and linking groups ... were all well known in the art ... Given the level of skill in the art, the recitation of an ECL label linked to a coreactant is sufficient to permit a person skilled in the art to recognize that Applicants were in possession of the claimed invention" (e.g., see 11/24/03 response, page 16, section 2).

[3] Applicants argue, "Examples are not required to meet the Written Description Requirement" and cite MPEP § 2163 in support of this position (e.g., see 11/24/03 response, page 16, section 3).

[4] Applicants argue, "In any Event, the Specification Provides Examples of Suitable Compounds" (e.g., see 11/24/03 response, pages 17-18, section 4).

[5] Applicants argue, "Many of the rejected claims specifically recite structural features" (e.g., see 11/24/03 response, pages 18-19, section 5).

[6] Applicants argue, "whether electrochemiluminescence occurs via singlet relaxation or via triplet-triplet annihilation is immaterial to the patentability of the claimed subject matter. The specification provided an empirical definition of what Applicants regard as electrochemiluminescence ... In both the relaxation or annihilation mechanisms, the reactions caused by exposure of the molecule to electrochemical energy must be sufficiently energetic to promote the ECL label to an excited state (e.g., either a singlet or a triplet state). Given the high level of skill in the art, the skilled practitioner will be able to predict on the basis of

electrochemical and spectroscopic properties whether the ECL label has such a state and whether it can be accessed by the application of electrochemical energy. Even in the absence of this information, the skilled practitioner has a wealth of data available on known ECL labels that work by either mechanism.

[7] Applicants argue, "The term coreactant [as currently amended] does not read on all compounds" (e.g., see 11/24/03 response, page 20, section 7)

Applicants' arguments have been fully considered but are not found persuasive for the following reasons:

[1] The Examiner respectfully disagrees. The "reasonable basis" for asserting that Applicants' invention does not meet the written description requirement is that Applicants' specification does note meet the standards set forth in *Lilly*, *Enzo* and MPEP § 2163.05 as outlined in the newly amended rejection above. In addition, the Examiner contends that Applicants have merely provided a "laundry list" of "potential" examples that would not reasonably lead a person of skill in the art to any particular species possessing the requisite functional properties (e.g., See, *Fujikawa v. Wattanasin*, 93 F.3d 1559,1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species). In addition, the "potential" examples of labels, linkers and coreactants that are set forth are not adequately described either because Applicants do not show how these compounds can be connected together to form the desired conjugates that will possess the desired functional properties (i.e., the coreactant will be oxidized and/or reduced and then subsequently react with the label to emit chemiluminescence) especially in light of the

unpredictability/variability that is known in the art (e.g., see amended rejection above, citations to Knight et al.).

[2 and 4] First, the Examiner contends that this argument fails to address the "unpredictability" and/or "variability" in the art as outlined in the amended rejection above (e.g., energy-deficient systems) and, as a result, Applicants' arguments are not commensurate in scope with the claims i.e., Applicants do not provide any examples of "energy-deficient" conjugates. Second, when there is little to no disclosure in the instant specification of the starting material or conditions under which claimed process can be carried out, this failure cannot be rectified by asserting that all disclosure related to the process is within skill of art. *Genentech Inc. v. Novo Nordisk A/S* (CA FC) 42 USPQ2d 1001 (3/13/1997). Third, the Examiner sets forth Knight et al. for the sole purpose of refuting Applicants' arguments that ecl labels, linkers and coreactants were well known in the art (e.g., see Knight, A.W.; Greenway, G.M. "Relationship between structural attributes and observed electrogenerated chemiluminescence (ECL) activity of tertiary amines as potential analytes for the tris(2,2-bipyridine)ruthenium" Analyst 1996, 121(11), 101R-106R), which clearly shows that even for a narrow subset of Applicants' most preferred embodiments great unpredictability/variability exists (e.g., see newly amended rejection above)).

[3] While an example is indeed not required, lack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art (see below). Also, one of ordinary skill would not necessarily expect to be able to extrapolate the disclosed example (e.g., a <u>few examples</u> of a tris-bipyridine ecl label conjugated via an alkylamine linker to several alkyl amine coreactants) as far as its applicability to the instant claims.

As noted in the amended rejection above, the Examiner deems the art to be unpredictable (e.g., see amended rejection above, energy deficient compounds; see also citations to Knight et al.). The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Additionally, the Board has held on the issue of unpredictability that "... the unpredictability of an art area alone may be enough to create a reasonable doubt as to the accuracy of statements in the specification." *Ex parte Singh*, 17 U.S.P.Q.2d 1714,1716 (B.P.A.I. 1990).

With respect to adequate disclosure of the scope of the presently claimed generic applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding disclosure. For adequate disclosure, like enablement, requires ***representative examples*** which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure. Finally, when there is substantial variation within the genus, one must

describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05).

Here, Applicants have not provided a "representative" number of examples and/or species that "reflect the variation within the genus" as required by MPEP § 2163.05 and *Lilly*. For example, Applicants' specification does not provide any examples and/or species of energy deficient systems that generate light emission via "forbidden" pathways (e.g., triplet-triplet annihilation), which would be included in Applicants' broad genus because Applicants do not "wish to be bound by a theoretical explanation of reaction mechanism" (see specification, page 11, lines 1-2). Furthermore, Applicants' teachings in the specification do not remedy this deficiency because the equation to which Applicants' refer for guidance (e.g., see specification, claims 12 wherein Applicants' disclose $\Delta G^0 = E^0(A/A-)-E^0(D+/D)$) does not apply to these energy deficient systems. In addition, the general knowledge and level of skill in the art do not supplement the omitted description either because these systems are highly "unpredictable" (e.g., see amended rejection above, citations to Knight et al.).

[5] The Examiner contends that the structural features that are missing in each of the dependent claims have been accounted for in the newly amended rejection above (e.g., "the ecl label (e.g., see claims 3, 4, 10-20, 26-38), linker (e.g., see claims 3, 4, 10-19, 26-27, 30-38) and/or coreactant (e.g., claims 3, 4, 10-13, 19-20, 26-35) are not structurally defined (or, in the alternative, are only "minimally" defined)."

[6] The Examiner respectfully contends that Applicants' statements (1) "the skilled practitioner will be able to predict ... whether the ECL label has such a state [i.e., triplet state] and whether it can be accessed by the application of electrochemical energy [i.e., react with

reduced/oxidized coreactant]" and (2) "the skilled practitioner has a wealth of data available on known ECL labels that work by either mechanism [e.g., triplet-triple]" are entirely unfounded. If Applicants possess such references that will allow a person of skill in the art to predict the structure of a compound that will fall within the scope of Applicants' claims that proceed via the triplet-triplet mechanism then Applicants should submit such a reference for consideration. In the absence of such evidence this line or reasoning is moot. Furthermore, Applicants arguments that "energy-deficient" systems are "immaterial to the patentability of the claimed subject matter" is also without merit because Applicants are claiming such compound and must show possession for the full scope of the claims.

[7] The Examiner agrees with Applicants' assessment of the newly amended claims, but reaffirms the written description rejection on the grounds cited in the newly amended rejection above.

Accordingly, the written description rejection cited above is hereby maintained.

12. Claims 3, 4, 10-20, 26-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific metal-tris-terpyridine complexes linked tertiary amines disclosed, does not reasonably provide enablement for ***any*** electrochemiluminescent "label" linked via ***any*** "linker" to ***any*** "coreactant." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use invention as broadly as it is claimed. This is an enablement rejection.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors may include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) Breadth of the claims and nature of the invention: Applicants' newly added claims are directed to a broad and highly diverse genus of electrochemiluminescent (ecl) conjugates comprising an "electrochemiluminescent label" linked presumably by a "linker" to a "coreactant" (e.g., see newly amended claim 3). These claims represent enormous scope because the ecl label (e.g., see claims 3, 4, 10-20, 26-38), linker (e.g., see claims 3, 4, 10-19, 26-27, 30-38) and/or coreactant (e.g., claims 3, 4, 10-13, 19-20, 26-35) are not structurally defined (or, in the alternative, are only "minimally" defined) and thus would include an enormous number of structural variants falling within virtually every known chemical class and subclass.

(3 and 5) The state of the prior art and the level of predictability in the art: The level of predictability in the art is low because there is a large variation in ecl activity even

between very closely related molecules like Applicants' most preferred tertiary amine embodiments (e.g., see Knight et al., page 101R, column 2, "It is not the case, however, that all tertiary amine compounds take part in ECL reactions with $Ru(bpy)_3^{2+}$ [i.e., one of Applicants' preferred embodiments e.g., see figure 1-2 in specification] to produce light. Many tertiary amine compounds produce intense emission whereas other structurally related similar compounds produce virtually no ECL emission") (emphasis added). Furthermore, Knight et al. indicate that a broader class of molecules could not easily be studied (e.g., see Knight et al., page 102R, column 1, first full paragraph, "practical difficulties arise if a range or family of compounds are to be compared to determine their relative ECL activity. Relatively small changes in the structure of compounds, e.g., a stepwise increase in alkyl chain length, will often dramatically change its solubility, [etc.] ... Hence comparisons over a range of compounds under the same experimental conditions are often not possible").

Furthermore, Knight et al. indicate that Applicants most preferred embodiments (i.e., $Ru(bpy)_3^{2+}$ linked to amines, e.g., see figures 1-2; see also claim 9) ***will not work*** unless the amine is positioned next to an α-carbon that contains a proton. Knight et al. state that a hydrogen atom attached to the α-carbon is "essential" for ECL activity (e.g., see Knight et al., Conclusion, "A hydrogen atom attached to the α-carbon is usually essential for ECL activity") because it is the α-carbon that forms the strongly reducing intermediate that is "the source of the chemical energy to produce ... the ECL reaction" (e.g., see Knight et al., paragraph bridging pages 102R-103R, Reaction Mechanism section; see also page 103R, figure 2) (emphasis added). In this regard, it is noted that claims which

lack critical or essential subject matter, which is necessary to the practice of the invention, but is not included in the claim(s), ***including essential compound structure***, is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976); and *Ex Part Bhide* (Bd Pat. App. & Int.) 42 USPQ2d 1441.

Finally, Knight et al. indicate that many other classes of compounds (outside of the preferred embodiments mentioned above) will not work. For example, Applicants claims encompass aromatic amines as co-reactants and Applicants' specification clearly states that aromatic amines like aniline can be used with the invention (e.g., see specification, page 13, paragraph 2, "The amine substance in the present invention can also be an aromatic amine, such as aniline."). However, Knight et al. clearly state that compounds like aniline will not work (e.g., see Knight et al., page 104R, first fully paragraph, "For example, no ECL is observed for aniline") because the conjugation and/or aromaticity "excessively stabilize" the radical intermediates.

(4) The level of one of ordinary skill: The level of skill required would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants disclose only a few examples of a tris-bipyridine ecl label conjugated via an alkylamine linker to several alkyl amine coreactants (e.g., see specification, Examples; see also figures 1-2; see also specification pages 13-14).

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: As a result of the broad and unpredictable nature of the invention and the lack of specific guidance from the specification, the Examiner contends

that the quantity of experimentation needed to make and or use the invention would be great. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 * n.23 (Fed. Cir. 19991). In this case, Applicants have provided only a limited number of closely related examples that would not teach this enormous genus that falls within a highly unpredictable art area. In addition, Applicants have omitted essential subject matter from the claims in violation of *In re Mayhew* (see sections 3 and 5 above). Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Response

13. Applicant's arguments directed to the above Enablement rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "Applicants respectfully disagree for the reasons set forth above" (e.g., see 11/24/03 response, page 21, paragraph 2).

[2] Applicants argue that they have provided enough examples in the specification and/or cited references to fully enable the claimed invention and cite various passages in the specification in support of this position (e.g., see 11/24/03 response, page 21, last two paragraphs; see also page 22, last two paragraphs).

[3] Applicants argue the Knight et al. reference exemplifies a high level of skill in the art (e.g., see 11/24/03 response, page 23, middle paragraph).

[4] Applicants argue, "there is no requirement that an applicant provide a working example of his invention ... 35 USC § 112 requires nothing more than objective enablement ... [the] specification describes the present invention in broad terms and also provides numerous examples of specific preferred embodiments ... Applicants submit that it is improper to reject claims on the ground that the specification does not supper the claims when the terms are no broader than the broadest description of the invention in the specification and there is no reason to challenge the operativeness of the subject matter embraced by the claims" and cite *Ex Parte Altermatt* in support of this position (e.g., see 11/24/03 Response, pages 24-25).

[5] Applicants argue that because the relative skill of those in the art is high, the threshold point at which experimentation becomes undue must also be high. Given this, Applicants submit that, based on the instant specification one skilled in the art would not have to engage in undue experimentation in order to practice the claimed invention (e.g., see 11/24/03 Response, page 25, paragraphs 2-3).

[6] Applicants argue that their newly amended claims do not read on "all compounds" and that it would be within the skill of one in the art to prepare, use and test the virtually

unlimited number of compounds that are currently claimed (e.g., see 11/24/03 Response, page 25, paragraphs 1-2).

[7] Applicants argue that the Examiner's previous statements support the notion that the state of the prior art is high (e.g., see 11/24/03 Response, page 26, last two paragraphs).

[8] Applicants argue that it is "unclear" how the Examiner reaches the conclusion that the prior art is unpredictable (e.g., see 11/24/03 Response, page 27-28).

[9] Applicants argue that Knight et al. reference provides support for Applicants' assertion that ECL labels and coreactants were well known in the art and further states that several of the quotations cited by the examiner were misapplied. For example, Applicants state, "Knight II goes on to review the literature on amine coreactants and to form conclusions tying the activity of amine coreactants to certain structural features ... showing that, contrary to the Examiner's assertions, there is predictability in the selection of amine coreactants" (e.g., see 11/24/03 Response, page 38, middle two paragraphs).

This is not found persuasive for the following reasons:

[1] The Examiner contends that to the extent that the "above" arguments [i.e., made in the written description rejection] can be applied here, they have been adequately addressed in that rejection which is incorporated by reference herein in its entirety.

[2] The Examiner respectfully disagrees. As stated in the amended rejection above the claimed genus is enormous and highly variable. The Knight et al. reference (e.g., see Applicants' arguments, page 23, middle paragraph) clearly indicates that Applicants have not provided enough examples to enable their broad genus (e.g., see Knight, A.W.; Greenway, G.M. "Relationship between structural attributes and observed electrogenerated chemiluminescence

(ECL) activity of tertiary amines as potential analytes for the tris(2,2-bipyridine)ruthenium" Analyst 1996, 121(11), 101R-106R). Knight et al. indicate that Applicants' most preferred embodiments (i.e., $Ru(bpy)_3^{2+}$ linked to amines, e.g., see figures 1-2; see also claim 9) ***will not work*** unless the amine is positioned next to an α-carbon that contains a proton. Knight et al. state that a hydrogen atom attached to the α-carbon is "essential" for ECL activity (e.g., see Knight et al., Conclusion, "A hydrogen atom attached to the α-carbon is usually essential for ECL activity") because it is the α-carbon that forms the strongly reducing intermediate that is "the source of the chemical energy to produce ... the ECL reaction" (e.g., see Knight et al., paragraph bridging pages 102R-103R, Reaction Mechanism section; see also page 103R, figure 2) (emphasis added). Thus, a person of skill in the art would not be able to practice the claimed invention with an amine that does not possess an α-carbon with a hydrogen atom (i.e., a person of skill in the art would not even be able to practice the claimed invention within the relatively narrow scope of Applicants' most preferred embodiments i.e., $Ru(bpy)_3^{2+}$ with tertiary amines, let al.one the almost infinite number of compounds that are not included in the preferred embodiments that are considerable less predictable).

[3] The Examiner respectfully disagrees. Knight et el. proves that even for a narrow class of compounds i.e., bipyridine metal chelates used in conjunction with alkyl amines the art is highly variable and unpredictable (e.g., see amended rejection above). For example, Knight et al. indicate that Applicants most preferred embodiments (i.e., $Ru(bpy)_3^{2+}$ linked to amines, e.g., see figures 1-2; see also claim 9) ***will not work*** unless the amine is positioned next to an α-carbon that contains a proton. Knight et al. state that a hydrogen atom attached to the α-carbon is "essential" for ECL activity (e.g., see Knight et al., Conclusion, "A hydrogen atom attached to

the α-carbon is usually essential for ECL activity") because it is the α-carbon that forms the strongly reducing intermediate that is "the source of the chemical energy to produce ... the ECL reaction" (e.g., see Knight et al., paragraph bridging pages 102R-103R, Reaction Mechanism section; see also page 103R, figure 2) (emphasis added).

In addition, Knight et al. proves that other systems would be even more difficult to study than the alkyl amines disclosed (e.g., see Knight et al., page 102R, column 1, first full paragraph, "practical difficulties arise if a range or family of compounds are to be compared to determine their relative ECL activity. Relatively small changes in the structure of compounds, e.g., a stepwise increase in alkyl chain length, will often dramatically change its solubility, [etc.] ... Hence comparisons over a range of compounds under the same experimental conditions are often not possible"), thus refuting Applicants' arguments that the teachings in Knight could be extended to other systems.

[4] With respect to an argument that an example is not necessary, applicant is directed to MPEP § 2164.02. Lack of a working example (or examples) is a factor to be considered, especially in a case involving an unpredictable and undeveloped art. While it is true that an example is not required, it is often necessary to provide description and enablement for broad claims. Thus, in applications directed to invention in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). Furthermore, the Examiner has set forth several "reason[s] to challenge the operativeness" of the claimed invention using, for example, the Knight et al. reference (e.g., see amended rejection above).

[5] First, the Examiner notes that when there is little to no disclosure in the instant specification of the starting material or conditions under which claimed process can be carried out, this failure cannot be rectified by asserting that all disclosure related to the process is within skill of art. *Genentech Inc. v. Novo Nordisk A/S* (CA FC) 42 USPQ2d 1001 (3/13/1997). Second, the Examiner contends that "skill in the art" is only one of many factors to consider and the vast majority of factors (e.g., see Wands analysis above) indicate that undue experimentation would be required (i.e., Applicants provide little guidance but claim enormous scope in a highly diverse and unpredictable art area).

[6] The Examiner agrees that Applicants' newly amended claims do not encompass "all" compounds, but this doesn't lessen the egregious nature of the scope problem because Applicants' claims still read on virtually an unlimited number. In addition, Applicants claims encompass a highly diverse genus (e.g., see amended rejection above, section Wands factors (1-2) above).

[7-8] The Examiner has amended the original rejection to more clearly address Applicants' concerns, which further proves that undue experimentation would be required (e.g., see newly amended section (3 and 5) above).

[9] The Examiner respectfully disagrees. The Knight et al. reference clearly indicates that their is enormous variability even within a very very small subgenus (i.e., Applicants' preferred amines) of the claimed invention. The fact that Knight et al. were able to make some limited predictions regarding the small subgenus doesn't speak to the enormous number of currently claimed compounds and Knight et al. explicitly state that those compounds would be very difficult to test and that no such studies have been performed on that magnitude (i.e., the

Knight study was limited to only alkylamines). Furthermore, Knight et al. explicitly state that even within the very limited number of closely related labels and coreactants used, many of the compounds did not work. For example, Knight et al. state that a hydrogen atom attached to the α-carbon is "essential" for ECL activity (e.g., see Knight et al., Conclusion, "A hydrogen atom attached to the α-carbon is usually essential for ECL activity") because it is the α-carbon that forms the strongly reducing intermediate that is "the source of the chemical energy to produce ... the ECL reaction" (e.g., see Knight et al., paragraph bridging pages 102R-103R, Reaction Mechanism section; see also page 103R, figure 2) (emphasis added). Here, Applicants' claims lack this critical hydrogen attached to the α-carbon (i.e., Applicants' claims lack the critical α-proton structure). In this regard, it is noted that claims which lack critical or essential subject matter, which is necessary to the practice of the invention, but is not included in the claim(s), ***including essential compound structure***, is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976); and *Ex Part Bhide* (Bd Pat. App. & Int.) 42 USPQ2d 1441.

Accordingly, the Enablement rejection cited above is hereby maintained.

Claims Rejections - 35 U.S.C. 102

14. Claims 3-4, 10, 12-13, 18-20, 26-27 and 29-35 and 40 are rejected under 35 U.S.C. 102(a) as being anticipated by Liang et al. (Liang, P.; Dong, L.; Martin, M. T. "Light Emission from Ruthenium-Labeled Pencillins Signaling Their Hydrolysis by β-Lactamase" *J. Am. Chem. Soc.* **1996**, *118*, 9198-9199). 3, 4, 10-20, 26-38

For ***claims 3-4, 10, 12-13, 18-20, 26-27, 29-35 and 40***, Liang et al. disclose a $Ru(bpy)_3^{2+}$-labeled 6-Aminopenicillanic Acid (Ru-APA) that is hydrolyzed by a β-lactamase (see Liang et al., page 9199, Figures 1 and 2), which reads on all the limitations in claims 3-4, 10, 12-13 and 18-22 because the Ru-APA contains a Ruthenium complex electrochemiluminescent label and a coreactant with a hydrolyzed β-lactam bond.

Response

15. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue that Liang is not prior art because Applicants are entitled to a priority of June 7, 1995, which is the filing date of parent application Serial No. 08/485,419 (e.g., see 11/24/03 Response, page 31, paragraph 1-2).

This is not found persuasive for the following reasons:

The Examiner contends that Applicants are not entitled to the June 7, 1995 priority and, as a result, Applicants arguments are moot (e.g., see Priority section above).

Accordingly, the 35 U.S.C. § 102 rejection cited above is hereby maintained.

16. Claims 3, 11, 13, 14, 31-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Faulkner, L. R. (Faulkner L. R. "Chemiluminescence from Electron-Transfer Processes" *Methods in Enzymology* (ed. by Marlene A. Deluca) **1978**, *17*, 494-526).

For ***claim 3, 11, 13, 14, 31-35***, Faulkner disclose a compound which comprises an electrochemiluminescent label (anthracene acceptor) linked via a methylene chain to a coreactant (N,N-dimethylaniline donor) which emits electrochemiluminescence when exposed to electrochemical energy (see Faulkner, page 507, third paragraph with structure) ("Annihilation of the ions gives emission from the ***intramolecular*** exciplex"), which anticipates claims 3, 11, 13, 14 because the coreactant (N,N-dimethylaniline) is not an analyte of interest and the coreactant is a tertiary amine.

Although, the publication does not state that oxidation/reduction reactions occur as stated in steps (i) and (ii) of claims 3-4, the Examiner contends that these properties would be inherent because the same structure as that which is currently claimed by Applicants is disclosed (e.g., see above). Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01.

In addition, the Examiner notes that the dimethylaniline contains the requisite hydrogen at the α-carbon adjacent to the nitrogen (e.g., compare to Knight et al., page 103R, figure 1) and, as a result, would also be able to undergo oxidation and subsequent deprotonation to form the requisite claimed "strong reductant" i.e., (C_6H_6)-N-(CH_3) [the other methyl group attached to the

nitrogen is not shown] → (C_6H_6)-N*-(CH_3) [oxidized species - 1 electron] → (C_6H_6)-N-$(CH_2$*) just as the compounds in Knight et al. do.

Response

17. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "First, the Examiner incorrectly characterizes anthracene and dimethylaniline as separate label and coreactant components. Faulkner states that the emission comes from an intramolecular exciplex comprising both anthracene and dimethylaniline (e.g., see 11/24/03 Response, pages 31-32).

[2] Applicants argue, "Even assuming, for the sake of argument, that the dimethylaniline can be described as a separate coreactant, the compound of Itaya and Toshima would be expected to require oxidation of the luminophore and concurrent reduction of the dimethylaniline moiety to provide a strong reductant, not a strong oxidant (see the mechanism on p. 507 of Faulkner). By contrast, the coreactants of amended Claims 3 and 4 require a coreactant that undergoes oxidation to form a reductant or reduction to form an oxidant ... The Examiner's contention that 'it does not rule out the possibility that the compound could also undergo the mechanism claimed by Applicant' ... is unsupported by evidence" (e.g., see 11/24/03 Response, page 32, middle paragraph).

[3] Applicants argue, "Scientific literature ... refutes the Examiner's position. Knight II notes that aniline and a variety of substituted anilines do not work as coreactants for generating ECL from $Ru(bpy)_3$" (e.g., see 11/24/03 Response, page 32, last paragraph).

[4] Applicants argue that there is no reasonable basis to make an "inherency" argument and cite Ex Parte Levy, Ex Parte Skinner, In re Robertson, etc. in support of this position.

This is not found persuasive for the following reasons:

[1] In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "separate ECL coreactant present") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Here, Applicants' arguments are not commensurate in scope with the claims. Applicants use "comprising" terminology that does not preclude the formation of an exciplex.

[2] The Examiner contends that the structure of dimethyl aniline falls within Applicants current claims and also within their most preferred embodiments and thus would be expected to inherently possess the claimed functions e.g., the co-reactant is an amine which falls not only within generic claims 3 and 4, but also dependent claims, which represents Applicants' more preferred embodiments (e.g., claims 35). Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the

applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01.

In addition, the Examiner notes that the dimethylaniline contains the requisite hydrogen at the α-carbon adjacent to the nitrogen (e.g., compare to Knight et al., page 103R, figure 1) and, as a result, would also be able to undergo oxidation and subsequent deprotonation to form the requisite claimed "strong reductant" i.e., (C_6H_6)-N-(CH_3) [the other methyl group attached to the nitrogen is not shown] → (C_6H_6)-N*-(CH_3) [oxidized species - 1 electron] → (C_6H_6)-N-(CH_2*) just as the compounds in Knight et al. do. Thus, the Examiner's position is now clearly "supported" by the Knight et al. reference.

Finally, the Examiner notes that Applicants have not provided any data indicating that the compounds disclosed in Faulkner will not undergo the requisite transitions. Applicants' arguments do not rise to the level of factual evidence. See MPEP § 716.01(c): The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965).

[3] The Examiner respectfully disagrees. The reference never states that "dimethylaniline", the compound in question, does not work. It only states that "aniline, diphenylamine and triphenylamine" do not work (e.g., see Knight et al., 104R, column 1, first full paragraph). However, none of these compounds contain the required hydrogen bearing "alkyl" α-carbon (as does dimethylaniline) that allows for the formation of a strong reducing agent upon deprotonation (e.g., see Knight et al., paged 103R, figure 1). Thus, Applicants arguments are moot because they are comparing apples with oranges. In addition, the reference states that aromatic amines (to which dimethylaniline belongs) give "low ECL responses", which

would fall within the scope of Applicants' claims (i.e., the response is greater than zero). Again, the Examiner notes that Applicants' arguments do not rise to the level of factual evidence. See MPEP § 716.01(c): The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965).

In addition, the Examiner notes that Applicants' arguments contradict their own specification (e.g., see page 13, paragraph 2, "The amine substance in the present invention can also be an aromatic amine, such as aniline") (emphasis added). Thus, Applicants' interpretation of the Faulkner reference are not reasonable in light of the specification.

[4] The Examiner respectfully disagrees. The Examiner notes that the dimethylaniline contains the requisite hydrogen at the α-carbon adjacent to the nitrogen (e.g., compare to Knight et al., page 103R, figure 1) and, as a result, would also be able to undergo oxidation and subsequent deprotonation to form the requisite claimed "strong reductant" i.e., (C_6H_6)-N-(CH_3) [the other methyl group attached to the nitrogen is not shown] → (C_6H_6)-N*-(CH_3) [oxidized species - 1 electron] → (C_6H_6)-N-$(CH_2$*) just as the compounds in Knight et al. do. Therefore, the Examiner has provided the required "basis in fact and/or technical reasoning" in question via the Knight et al. reference. In addition, the Examiner notes that Applicants' specification is consistent with this interpretation of the Knight et al. reference (e.g., see page 13, paragraph 2, "The amine substance in the present invention can also be an aromatic amine, such as aniline") (emphasis added).

Accordingly, the 35 U.S.C. § 102 rejection cited above is hereby maintained.

18. Claims 3-4, 10-14 and 19-20, 26-27 and 29-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Massey et al. WO 87/06706 (Date of Publication is **November 5, 1987**).

For ***claim 3-4, 10-14, 19-20, 22, 26-27 and 29-36***, Massey et al. teach a metal containing ECL label linked to a coreactant (see Massey et al., pages 144, 189 and 193 showing a $Ru(bpy)_3$ linked to another $Ru(bpy)_3$ and digoxigenin, $Ru(bpy)_3$ linked to a primary amine, and $Ru(bpy)_3$ linked to a theophylline, respectively), which reads on the limitations in claims 3-4, 10-14 and 19-22. The Digoxigenin conjugate on page 144 meets the limitation of claim 11 wherein "the coreactant is not an analyte of interest" because the coreactant is a $Ru(bpy)_3$ i.e., both the coreactant and the electrochemiluminescent label are $Ru(bpy)_3$ groups, which generate light via the following mechanism $Ru(bpy)_3^{+} + Ru(bpy)_3^{3+} \rightarrow {}^*Ru(bpy)_3^{2+} + Ru(bpy)_3^{2+}$ (see Knight et al., page 884, equation 15) leaving the analyte of interest, digioxigenin or digioxigenin binding compounds, intact. Note: ${}^*Ru(bpy)_3^{2+}$ emits light.

Applicants specification states, "Amines which are advantageously utilized in the present invention are aliphatic amines, such as primary, secondary and tertiary alkyl amines, the alkyl groups of each having from one to three carbon atoms, as well as substituted aliphatic amines" (e.g., see specification, page 13, paragraph 2). Theophylline clearly falls within this definition as a "preferred" embodiment because it represent a "tertiary" alkyl amine (e.g., CH_3-N-$(C=O)_2$-ring-etc., see page 193). In addition, the compound listed on page 191 of Massey et al. also falls within this definition because it represents a "primary" alkyl amine (e.g., $Ru(bpy)_3^{2+}$-$(CH_2)_4$-NH_2). In addition, the $Ru(bpy)_3^{2+}$-$(CH_2)_4$-NH_2 contains the requisite alkyl α-hydrogen atom (e.g., $Ru(bpy)_3^{2+}$-(CH_2)-(CH_2)-(CH_2)-$(C\underline{\mathbf{H}}_2)$-$NH_2$), which can deprotonate as required by Knight

et al. (e.g., see Knight et al., page 103R, figure 1) to form a strong reducing agent (e.g., forms $Ru(bpy)_3^{2+}$-(CH_2)-(CH_2)-(CH_2)-$(C\underline{H}_1*)$-NH_2) after oxidation/deprotonation just as the primary alkyl amines reported in Knight et al. do. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01.

Response

19. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue that the Examiner has provided no "factual support" for the assertion that the properties disclosed by Massey would "inherently" meet the claimed limitations (e.g., see 11/24/03 Response, page 34).

This is not found persuasive for the following reasons:

The Examiner respectfully disagrees. Applicants specification states, "Amines which are advantageously utilized in the present invention are aliphatic amines, such as primary, secondary and tertiary alkyl amines, the alkyl groups of each having from one to three carbon atoms, as

well as substituted aliphatic amines" (e.g., see specification, page 13, paragraph 2). Theophylline clearly falls within this definition as a "preferred" embodiment because it represent a "tertiary" alkyl amine (e.g., CH_3-N-$(C=O)_2$-ring-etc., see page 193). In addition, the compound listed on page 191 of Massey et al. also falls within this definition because it represents a "primary" alkyl amine (e.g., $Ru(bpy)_3^{2+}$-$(CH_2)_4$-NH_2). In addition, the $Ru(bpy)_3^{2+}$-$(CH_2)_4$-NH_2 contains the requisite alkyl α-hydrogen atom (e.g., $Ru(bpy)_3^{2+}$-(CH_2)-(CH_2)-(CH_2)-$(C\underline{\mathbf{H}}_2)$-$NH_2$), which can deprotonate as required by Knight et al. (e.g., see Knight et al., page 103R, figure 1) to form a strong reducing agent (e.g., forms $Ru(bpy)_3^{2+}$-(CH_2)-(CH_2)-(CH_2)-$(CH_1{*})$-NH_2) after oxidation/deprotonation just as the primary alkyl amines reported in Knight et al. do.

Accordingly, the 35 U.S.C. § 102 rejection cited above is hereby maintained.

20. Claims 3-4, 10-14 and 19-20, 26-27 and 29-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Massey et al. (US Pat No. 5,591,581) (Date of Patent is **January 7, 1997**; Date Filed is **April 15, 1994**).

Claims ***3-4, 10-14, 19-20, 26-27 and 29-36*** are directed to a compound which is a ruthenium containing ECL labile linked via an amide bond to a coreactant which includes amines and teriary amines wherein the coreactant can be a strong oxidant or a strong reductant.

For claims, 3-4, 10-14, 19-20, 26-27 and 29-36 Massey et al. disclose electrochemiluminescent labels with a coordinated Re atom linked to numerous compounds 'B' where B can be peptides, nucleic acids, polysaccharides, alkaloids, steroids, vitamins, amino acids or non-biological polymers (see Massey et al., claim 1). Massey also teach amines linked

to ECL labels (see Massey et al., column 15, lines 1-15; column 30, lines 38-column 31 line 37). Note that proteins have amine groups as well e.g., lysine side chains, etc. and well as alkaloids, polysaccharides that contain amino pentose and hexose units, and amino steroids, which reads on claims 3-4, 10-12, 13-14 and 19-22.

For example, Applicants specification states, "Amines which are advantageously utilized in the present invention are aliphatic amines, such as primary, secondary and tertiary alkyl amines, the alkyl groups of each having from one to three carbon atoms, as well as substituted aliphatic amines" (e.g., see specification, page 13, paragraph 2). Here, the compound listed on column 15, lines 5-15 of Massey et al. clearly falls within this definition because it represents a "primary" alkyl amine (e.g., Metal complex-(CH_2)-$(CH_2)_n$-NH_2). In addition, the Metal complex-(CH_2)-$(CH_2)_n$-NH_2 contains the requisite alkyl α-hydrogen atom (e.g., Metal complex-(CH_2)-$(C\underline{H}_2)_n$-NH_2), which can deprotonate as required by Knight et al. (e.g., see Knight et al., page 103R, figure 1) to form a strong reducing agent (e.g., forms Metal complex-(CH_2)-$(C\underline{H}_1{}^*)_n$-NH_2) after oxidation/deprotonation just as the primary alkyl amines reported in Knight et al. do. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01.

21. Claims 3-4, 10-12, 13-14, 19-20, 26-27 and 29-36 are rejected under 35 U.S.C. 102(f) as being unpatentable over Massey et al. (US Pat No. 5,591,581) (Date of Patent is **January 7, 1997**; Date Filed is **April 15, 1994**). The claimed subject matter appears to have been invented by Massey et al.

Claims ***3-4, 10-12, 13-14, 19-20, 26-27 and 29-36*** are directed to an invention not patentably distinct from claims 1-6 and 20 of commonly assigned 5,591,581. Specifically the applicant's are directed to the teachings of Massey et al. '581 as applied under 35 USC 102(e) *supra*.

Response

22. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue that the Examiner has provided no "reasonable basis" for the assertion that the Massey disclose a "coreactant" (e.g., see 11/24/03 Response, page 35; see also similar arguments for 102(f) rejection on page 36).

This is not found persuasive for the following reasons:

The Examiner respectfully disagrees. Applicants specification states, "Amines which are advantageously utilized in the present invention are aliphatic amines, such as primary, secondary

and tertiary alkyl amines, the alkyl groups of each having from one to three carbon atoms, as well as substituted aliphatic amines" (e.g., see specification, page 13, paragraph 2). Clearly, the compounds denoted in claim 1 of Massey et al represent "amines" under this definition and, as a result of their structural similarity, would be expected to "inherently" possess the same functional features. In addition, the compound listed on column 15, lines 5-15 of Massey et al., for example, clearly falls within this definition because it represents a "primary" alkyl amine (e.g., Metal complex-(CH_2)-$(CH_2)_n$-NH_2). In addition, the Metal complex-(CH_2)-$(CH_2)_n$-NH_2 contains the requisite alkyl α-hydrogen atom (e.g., Metal complex-(CH_2)-$(C\underline{H}_2)_n$-NH_2), which can deprotonate as required by Knight et al. (e.g., see Knight et al., page 103R, figure 1) to form a strong reducing agent (e.g., forms Metal complex-(CH_2)-$(C\underline{H}_1{}^*)_n$-NH_2) after oxidation/deprotonation just as the primary alkyl amines reported in Knight et al. do. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01.

Accordingly, the 35 U.S.C. § 102(e) and § 102(f) rejections cited above are hereby maintained.

Claim Rejections - 35 USC § 103

23. Claims 3-4, 9-20 and 26-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knight et al. (Knight, A. W.; Greenway, G. M. "Occurrence, Mechanisms and Analytical Applications of Electrogenerated Chemiluminescence" *Analyst* **1994**, *119*, 879-890) in view of Faulkner, L. R. (Faulkner L. R. "Chemiluminescence from Electron-Transfer Processes" *Methods in Enzymology* (ed. by Marlene A. Deluca) 1978, *17*, 494-526).

Knight et al. teach a large number of electrochemiluminescent compounds including $Ru(bpy)_3^{2+}$ complexes (e.g., see Knight et al., page 880, Table I, ruthenium complexes). Knight also teach a large number of coreactants including trialkylamines, NADH (e.g., see Knight et al., page 882, Table II, references 67, 79). Knight et al. also teach that ECL/coreactants can be used to detect biomolecules including amino acids, peptides and proteins (e.g., see Knight et al., page 884, column 2, line 12) and DNA (see Knight et al. page 883, Table II, reference 82).

The prior art teachings of Knight et al. differ from the claimed invention as follows:

The claimed invention differs from the prior art teaching of Knight et al. by reciting the advantages to be gained by linking an EL with a CR.

However, Faulkner teaches the following limitations that are deficient in Knight et al.:

Faulkner does teach the advantages to be gained by linking an EL with a CR by describing the work of Itaya and Toshima which provides an example of an anthracene linked to an N,N-dimethylaniline.

It would have been *prima facia* obvious to one having ordinary skill in the art at the time the invention was made to combine the teachings of Knight et al. with Faulkner as outlined above because both papers disclose compounds for electrogenerated chemiluminescence (i.e.,

each paper encompasses overlapping subject matter e.g., both papers show the use of anthracene and tertiary aromatic amines in electrogenerated chemiluminescence).

Furthermore, one of ordinary skill in the art would have been motivated to use the EL and CR compounds as taught by Knight with a linker to join the EL with the CR as taught by Faulkner because Faulkner specifically states the "advantages" of linking an EL to a CR (see Faulkner, pages 507-508) ("The linked systems [provide] an unusually efficient exciplex emission ... Note also that [the linked exciplex] is stabilized in a polar medium, rather than being destabilized as true exciplexes are. It is not surprising [i.e., it's obvious] that its chemiluminescence is very much brighter than that from the usual exciplex systems in polar solvents). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Faulkner et al. shows a working example of applicant's invention e.g., the anthracene linked to the N,N-dimethylaniline via a methylene chain (e.g., see Faulkner, page 507, third paragraph).

Response

24. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[a] Applicants argue, "As discussed above in Section IV(E), the cited compound in Faulkner does not comprsie a separate label and coreactant, but rather only the label, the obseved

emission being derived from an exciplex involving both the anthracene and the dimethylaniline ring structures" (e.g., see 11/24/03 Response, page 37, paragraph 2).

[b] Applicants argue, "There is no evidence of record to support an assertion that dimethylaniline can act as a coreactant that undergoes oxidation to form a reductant or reduction to form an oxidant" (e.g., see 11/24/03 Response, page 37, paragraph 3).

[c] Applicants argue, "Furthermore, neither Knight I nor Faulkner predict the unexpectedly high ECL efficiency that was obtained by linking such coreactants to ECL labels, nor do they provide any motivation for carrying out such a linkage" and cite cases including *In Re Dow Chemical Co.*, *Pro-Molde & Tool Co.*, *In re Dembiczak* in support of this position (e.g., see 11/24/03 Response, pages 37-38).

This is not found persuasive for the following reasons:

[a] The Examiner contends to the extent that Applicants arguments in Section IV(E) are being reapplied here, those arguments have been adequately addressed in that section and is incorporated in its entirety herein by reference (see above).

[b] In response to applicants' arguments against the Faulkner reference individually (i.e., the reference that discloses dimethylaniline), one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

[c] In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some

teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one of ordinary skill in the art would have been motivated to use the EL and CR compounds as taught by Knight with a linker to join the EL with the CR as taught by Faulkner because Faulkner specifically states the "advantages" of linking an EL to a CR (see Faulkner, pages 507-508) ("The linked systems [provide] an unusually efficient exciplex emission ... Note also that [the linked exciplex] is stabilized in a polar medium, rather than being destabilized as true exciplexes are. It is not surprising [i.e., it's obvious] that its chemiluminescence is very much brighter than that from the usual exciplex systems in polar solvents). In addition, the Examiner notes "there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention" (see MPEP § 2144).

Accordingly, the 35 U.S.C. § 103(a) rejection cited above is hereby maintained.

25. Claims 3-4, 9-20, and 26-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knight et al. (Knight, A. W.; Greenway, G. M. "Relationship between structural attributes and observed electrogenerated chemiluminescence (ECL) activity of tertiary amines as potential analytes for the tris(2,2-bipyridine)ruthenium(II) ECL Reaction" *Analyst* **1996**, *121*, 101R-106R) in view of Faulkner, L. R. (Faulkner L. R. "Chemiluminescence from Electron-Transfer Processes" *Methods in Enzymology* (ed. by Marlene A. Deluca) **1978**, *17*, 494-526).

Knight et al. teach electrochemiluminescent compounds including $Ru(bpy)_3^{2+}$ complexes (see Knight et al., page 101R, abstract). Knight also teach coreactants including tertiary amines

like tripropylamine (see Knight et al., page 103R, column 2, first paragraph). Knight et al. also teach that ECL/coreactants can be used to detect biomolecules including pharmaceuticals, amino acids and antibiotics (see Knight et al., page 101R, column 2, paragraph 3,). Knight et al. further teach Applicants reaction mechanism wherein the coreactant i.e., the tertiary amine undergoes oxidation or reduction to form a reductant or oxidant, respectively (see Knight et al., page 101R, column 2, paragraph 3; see also 102R, reaction mechanism section).

The prior art teachings of Knight et al. differ from the claimed invention as follows:

Knight et al. do not teach the advantage of linking an EL with a CR.

However, Faulkner teaches the following limitations that are deficient in Knight et al.:

However, Faulkner does teach the advantages to be gained by linking an EL with a CR by describing the work of Itaya and Toshima which provides an example of an anthracene linked to an N,N-dimethylaniline.

It would have been prima facia obvious to one having ordinary skill in the art at the time the invention was made to combine the teachings of Knight et al. with Faulkner as outlined above because both papers disclose compounds for electrogenerated chemiluminescence (i.e., each paper encompasses overlapping subject matter e.g., both papers show the use of an EL and a CR in electrogenerated chemiluminescence).

Furthermore, one of ordinary skill in the art would have been motivated to use the EL and CR compounds as taught by Knight et al. (i.e., the $Ru(bpy)_3^{2+}$ complexes with tripropylamine) with a linker to join the EL with the CR as taught by Faulkner because Faulkner specifically states the "advantages" of linking an EL to a CR (see Faulkner, pages 507-508) ("The linked systems [provide] an unusually efficient exciplex emission ... Note also that [the linked

exciplex] is stabilized in a polar medium, rather than being destabilized as true exciplexes are. It is not surprising [i.e., it's obvious] that its chemiluminescence is very much brighter than that from the usual exciplex systems in polar solvents). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Faulkner et al. shows a working example of applicant's invention e.g., the anthracene linked to the N,N-dimethylaniline via a methylene chain (see Faulnker, page 507, third paragraph) and Knight et al. teach that tripropylamine would be an excellent candidate to "link" to the $Ru(bpy)_3^{2+}$ (see Knight et al., page 103R, column 2, paragraph 1, "Tripropylamine has proved to be perhaps the most efficient amine for this ECL reaction, and is commonly used as a standard by which to compare the ECL activity of other amines"; please note that Applicants preferred embodiments are drawn to teriary amines including tripropylamine "linked" to $Ru(bpy)_3^{2+}$).

Response

26. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue, "The present invention claims priority to U.S.S.N. 08/484,766 filed June 7, 1995. The Knight II reference was published in November 1996 subsequent to the priority date of the subject application. Therefore, Knight II is not available as prior art" (e.g., see 11/24/03 Response, page 42, section M).

This is not found persuasive for the following reasons:

The Examiner contends that Applicants have not been afforded a priority date of June 7, 1995 for U.S.S.N. 08/484,766 (see priority section above) and, as a result, Applicants' arguments are moot.

Accordingly, the 35 U.S.C. § 103(a) rejection cited above is hereby maintained.

Double Patenting

27. Claims 3-4, 9-20 and 26-38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 19-20 of U.S. Patent No. 5, 591,581. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 3 and 4 are directed to a compound which is a metal containing ECL labile linked to a coreactant because Massey et al. disclose electrochemiluminescent labels with a coordinated Re atom linked to numerous compounds (B) where B can be peptides, nucleic acids, polysaccharides, alkaloids, steroids, vitamins, amino acids or non-biological polymers (see claim 1 for example). As a coreactant includes precursor species and species which upon the chemical transormation which result in species which can interact with the label to induce electrochemiluminescence Massey et al. anticipates claims 3-4, 9-20 and 26-83.

In addition, U.S. Patent No. 5,591,581 also amines linked to ECL labels (e.g., see column 15, lines 5-15.

Response

28. Applicant's arguments directed to the above double patenting rejection were fully considered but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue, Massey "as discussed above in Section IV(G)" does not anticipate the claimed invention and cite MPEP § 804 in support of this position, which states that a comparison of the claims must be made (e.g., see 11/24/03 Response, pages 38-39).

This is not found persuasive for the following reasons:

The Examiner contends that Massey et al. do disclose, in the claims as required by MPEP § 804, Applicants' claimed invention (e.g., see Response to Section IV(G) which is incorporated in its entirety herein by reference) and, as a result, Applicants' arguments are moot.

Accordingly, the double patenting rejection cited above is hereby maintained.

29. Claims 3-4, 9-20, 22 and 26-38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 5,643,713. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: Compounds which comprise an electrochemiluminescent label linked to a coreactant as set forth in claims 3 and 4 of the instant application are substantially identical if not identical

to those set forth in US 5,643,713, claims 1 and 6, although recited in slightly different language or by structure. One of ordinary skill in the art would recognize that the coreactant as recited in claims of the instant application are equivalent to the chemically transformable first compound as set forth in claim 1 of the 5,643,713 patent and have the properties recited in section I of the claim and undergo the reaction as set forth in section II of the claim.

Furthermore, there is no apparent reason why applicants were prevented from presenting claims corresponding to those of the instant application during prosecution of the application that matured into a patent. See In re Schneller, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

In addition to the teachings previously recited note that claim 6 recites an aromatic coreactant.

Response

30. Applicant's arguments directed to the above double patenting rejection were fully considered but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue, "With respect to the Liang '713 patent, Applicants have previously advised during the prosecution of the parent application that they are willing to provide a terminal disclaimer" (e.g., see 11/24/03 Response, pages 38-39).

This is not found persuasive for the following reasons:

The Examiner contends that Applicants have acknowledged their duty to file a terminal disclaimer, but have failed to do so.

Accordingly, the double patenting rejection cited above is hereby maintained.

New Rejections

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

31. Claims 3, 4, 9-20, 26-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

AA. For **claims 3 and 4**, the claims are indefinite because it is not clear whether Applicants are trying to claim more than one statutory class of invention (i.e., a product and a method of use) simultaneously? For example, the electrochemiluminescent label that is linked to a coreactant in claim 3 would appear to be a compound. However, steps (i) and (ii) recited in claim 3 would appear to be "method of use" steps because the compound is "exposed" to electrochemical energy and then subsequently "reacted" with a label to emit electrochemiluminescence (e.g., see newly amended claim 3) i.e., Applicants are claiming active method steps.

Please note that other "statutory hybrid" claims are not rejected like product-by-process claims because Applicants make clear what is being claimed i.e., the product (e.g., see MPEP § 2173.05(p), "A claim to a device, apparatus, manufacture, or

composition of matter may contain a reference to the process in which it is intended to be used without being objectionable under 35 U.S.C. 112, second paragraph, so long as it is clear that the claim is directed to the product and not the process"). Thus, the claim must "make clear" which statutory class of invention is being claimed (emphasis added). Here, Applicants have failed to "make clear" whether they are claiming a product or a process of use because several of the limitations cited above can reasonably be interpreted as method of use steps.

Furthermore, even if *assuming arguendo* that Applicants' method steps could be interpreted as "characteristics and/or properties" as purported, it is still unclear what structural limitations (if any) would be imparted to said compounds by such limitations. For example, claim 3 specifies, "on exposure of said compound to electrochemical energy ... [said compound will] form said reductant or said oxidant" which is merely a statement of one sought for property (i.e., the ability to form said reductant or said oxidant upon exposure to light) but tells nothing of the material to be employed (i.e., what physical characteristics will impart such properties). Similarly, claim 3 further recites, "said reductant or oxidant reacts with said label so as to cause said label to emit electrochemiluminescence," which again tells nothing of the material but only of one desired property thereof. Thus, Applicants define said compound solely in terms of what the compound does and not what it is. It is well settled that claiming only a result fails to satisfy the constitutional requisite of promoting the progress of science and the useful arts since this seeks to monopolize all possible ways to achieve a given result, far beyond those means actually discovered or contemplated by the inventor, so that others would

have no incentive thereafter to explore a field already fully dominated. *O'Reilly v. Morse*, 15 How. 62, *In re Fuetterer*, 50 CCPA 1453, 1963 C.D. 620, 795 O.G. 783, 319 F.2d 259, 138 USPQ 217 ; *Siegel v. Watson*, 105 U.S. Appl. D.C. 344, 1959 C.D. 107, 742 O.G 863, 267 F.2d 621, 121 USPQ 119. A material defined, as here, solely in terms of what it can do, does not particularly point out, as required by 35 U.S.C. 112, Applicants' disclosed invention. A person of skill in the art cannot immediately envision all the possible chemical structures for a peptide with this function. Thus, the metes and bounds of the claimed invention cannot be determined. See *ex parte Pulvari* (POBA 1966) 157 USPQ 169.

Response

32. To the extent that Applicants arguments against the previous 35 U.S.C. 112 second paragraph rejections can be applied to the new rejection, Applicants arguments are addressed below.

AA. **[1]** Applicants argue, "Given the detailed description in the specification of ECL coreactants (through examples, functional definition, lists of suitable coreactants and references to appropriate literature), the substantial body of literature that was available on ECL coreactants at the time of the invention, and the high level of skill in the art, Applicants urge that one of ordinary skill in the art would readily understand the meaning of the term "coreactant" (e.g., see 11/24/03 Response, page 29, middle paragraph).

[2] Applicants state that their newly amended claims do not read on "any" compound (e.g., see 11/24/03 Response, page 29, last paragraph).

[3] Applicants argue that there is "no requirement" that claimed compound be descried through the use of a structure as opposed to a function and cite MPEP § 2173.05(t) in support of this position.

This is not found persuasive for the following reasons:

AA. **[1]** The Examiner contends that Applicants are merely reciting a "desired" result, but that result does not indicate what structure the claimed compounds are to possess. The Examiner notes that Applicants have not set forth any structure/function relationship and, as a result, there is no way to extend Applicants' examples to other compounds because there is no relationship to do it. The fact that Applicants can test these compound via trial and error does not change the fact that Applicants are merely claiming a desired result because any desired result could always be tested by trial and error (e.g., See, *Fujikawa v. Wattanasin*, 93 F.3d 1559,1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species).

[2] The Examiner agrees with this assessment that the newly amended claims don't read on any compound, but does not agree that a person of skill in the art could readily determine whether a particular compound is or is not within the scope of the claims for the reasons outlined in the above rejection (e.g., see *In re Mercier*, 185 USPQ 774 (C.C.P.A. 1975).

[3] The Examiner agrees with Applicants' assessment of the law, but contends that such an accusation (i.e., that functional language is per se invalid) has never been made. Conversely, the Examiner is arguing that Applicants cannot claim that all functional language is permissible just because a per se rule against functional language has been upheld. Applicants' functional language may, in this case, impart some structural limitations but, as noted above, it is simply not clear what those limitations would be because there is no structure/function relationship for the vast majority of claimed compounds, nor is there any other "identifying" characteristics that would remedy this deficiency for the "full scope" of the claimed invention. In addition, Applicants have not set forth and conditions under which these compounds are to be tested. Thus, the metes and bound of the claimed invention cannot be determined.

Claims Rejections - 35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

33. Claims 3, 4, 10-15, 19, 26-37 are rejected under 35 U.S.C. 102(b) as being anticipated by DiCesare et al. (DiCesare, J.; Grossman, B.; Katz, E.; Picozza, E.; Ragusa, R.; Woudenberg, T. "A high-sensitivity Electrochemiluminescence-Based Detection System for Automated PCR Product Quantitation" BioTechniques **1993**, 15, 152-157).

For ***claim 3-4 and 32-34***, DiCesare et al. disclose TBR incorporated into a nucleic acid either at the 5' or 3' positions (e.g., see DiCesare et al., figure 2; see also page 153, column 2, Table at top of page showing PC03, 19A(C)A, 19A(C)B, etc.). Applicants do not state that their claimed compounds (either TBR alone or incorporated into various nucleic acids) undergo oxidation and/or reduction to form excited species that subsequently react with one another to produce electrochemiluminescence as outlined in steps (i) and (ii) of claims 3-4. However, DiCesare et al. teach that "typical" ECL reactions include "mixing appropriate chemical reagents which react to form an excited-state species that decays to the ground state and emits light ... [For example] ... Both the TBR label and a reactant, TPA [i.e., Applicants' preferred embodiment, compare to figures 1-2 in specification], which is added by means of the assay buffer, are oxidized. The oxidized TPA is converted to an unstable, highly reducing intermediate that then reacts with the oxidized TBR label, converting it to its excited-state form ... with the emission of light at 620 nm" (e.g., see paragraph bridging pages 153-154), which would encompass the steps (i) and (ii) of claims 3-4. In addition, DiCesare et al. do not add TPA in their experiments as outlined in the typical experiments (e.g., see Materials and Methods for buffer composition), but instead incorporate the ECL label, TBR, into either the 5' or 3' end of the nucleic acid primer which is then subsequently washed without TPA before detection (e.g., see page 155, column 1, first full paragraph). Thus, the nucleic acid primer itself must inherently be functioning as a highly reducing "TPA substitute" to generate the light emission at 620 nm (i.e., something still has to reduce the

TBR and it can't be the TPA because it wasn't added). Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01.

In addition, Dicesare et al. disclose TBR by itself (i.e., not incorporated into a nucleic acid (e.g., see figure 2), which also anticipates the claimed invention. Here, the label is tris (2,2'-bipyridine) ruthenium (II) chelate, the linker is $-(CH_2)_4-$ and X = -O-$P(CH_2CH_2CN)$-N-$(iPr)_2$. Although, the publication does not state that TBR undergoes the oxidation/reduction reactions stated in steps (i) and (ii) of claims 3-4, the Examiner contends that these properties would be inherent because TBR contains the same structure as that which is currently claimed by Applicants and that is also currently exemplified as their preferred embodiments (e.g., compare figure 2 of Dicesare et al. to figures 1-2 of Applicants' specification; compare also to claims 3-4 and especially claims 14-15 wherein Applicants and Dicesare et al. both disclose a bipyridine ruthenium (II) chelate conjugated to a dipropyl amine). In addition, the Examiner notes that TBR contains an α-carbon with a proton and thus would be able to undergo the required deprotonation to form the highly reducing radical species (e.g., see Knight et al., page 103R, figure 1). Where the claimed and prior art products are identical or substantially

identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01.

For ***claim 11, 31***, DiCesare et al. disclose TBR which does not contain a nucleic acid biomolecule analyte (e.g., see DiCesare et al., figure 2)

For ***claims 10, 12-15 27, 29-30, 35-37***, DiCesare et al. disclose nucleic acid biomolecules (e.g., see DiCesare et al., page 153, column 2, primers listed at top of page), which contain various amines (e.g., cytosine contains an $-NH_2$ attached to the C4 position and adenine contains an $-NH_2$ at the C6 position; A, C, G and T also contain various ring amines i.e., N1, N3, N7 and N9). In addition, DiCesare et al. disclose that the label is linked to the coreactant via the 5' or 3' -OH functional group of the nucleic acid. DiCesare et al. also disclose TBR contains a tertiary alkyl amine (e.g., see figure 2 wherein X = $-O-P-(CH_2-CH_2CN)-\underline{N-(iPr)_2}$).

For ***claims 19, 26***, Dicesare et al. disclose a single ruthenium ion (e.g., see figure 2).

For ***claim 28***, Dicesare et al. disclose the use of a "polyT" linker to attach the label to the nucleic acid primer at the 3' end (e.g., see page 153, column 2, Table at top of page wherein 19A(C)B is disclosed).

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
October 12, 2004

BENNETT CELSA
PRIMARY EXAMINER